



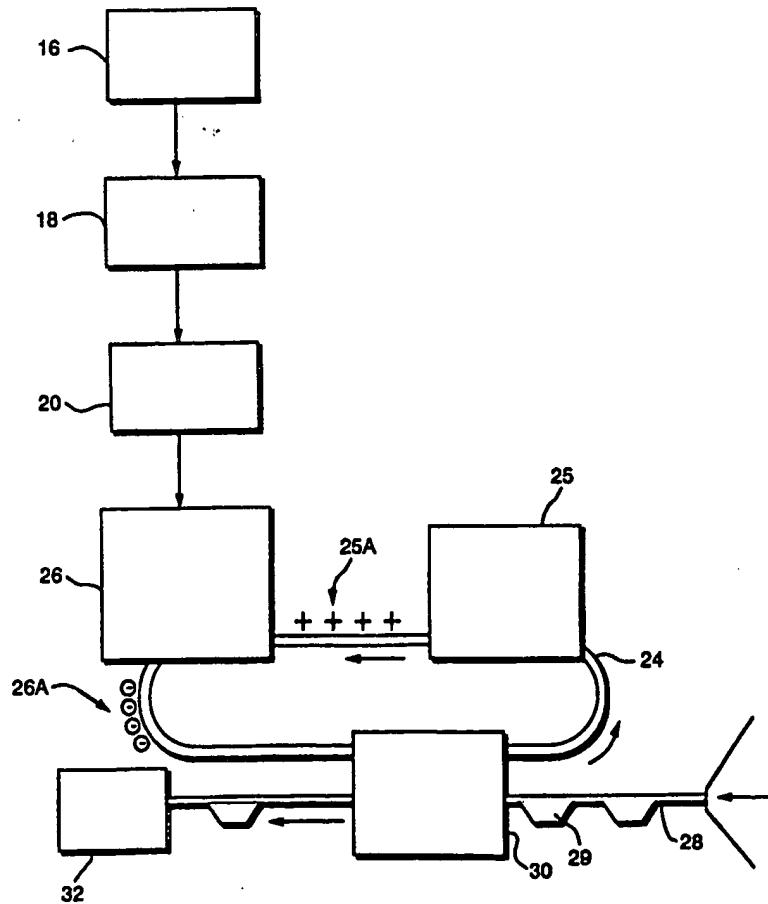
## INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

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## (54) Title: METERING AND PACKAGING DEVICE FOR DRY POWDERS

## (57) Abstract

Electrostatic phototechnology is used to meter and package microgram quantities of fine powders such as drugs. An electrostatic "image" (25A) having a given size and charge density is exposed to ionized drug powder (10) to attract a known precise amount of drug to the image. The resultant drug "image" (26A) is then transferred to a package (32).



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## METERING AND PACKAGING DEVICE FOR DRY POWDERS

1

2        The present invention relates to the packaging of dry powders and particularly  
3        to the packaging of microgram quantities of powders for medical uses. In the  
4        metering and packaging of dry powders, particularly very small amounts of dry  
5        powder medications, the drug industry has had difficulty with the packaging of  
6        precise amounts of such powders. One of the reasons for this is that many powders  
7        develop an electrical charge and the charge causes problems in measuring and  
8        packaging since powders tend to aggregate and stick to the sides of the containers and  
9        metering devices. The present invention utilizes this ability of the powder to acquire  
10       an electrical charge for precisely measuring exact microgram quantities of the powder  
11       and then placing these exact microgram quantities in individual containers.

12       In the past, technology has been used employing electrostatic charge to attract  
13       a given quantity of powder to a surface. An example of this is the laser printer or the  
14       electrostatic copy devices where a drum is charged and toner particles are attracted  
15       and held in position by the charge. The charge on the drum is neutralized by the  
16       attracted toner powder, thus limiting the amount of toner in accordance with the  
17       charge image on the drum. The charge on these printer drums is then transferred to a  
18       sheet of paper or other carrier to give a final image.

19       In the present invention, the same technology is employed for transferring a  
20       predetermined amount of a finely powdered medication to a carrier or an intermediate  
21       such as a drum, carrying a charge of predetermined intensity and area, rotating the  
22       charged drum surface, carrying the predetermined amount of powdered medication on  
23       its surface, to a transfer station where the charge is overcome and the dry powder is  
24       transferred to a package which is then sealed. In lieu of a drum, a belt, or other  
25       movable surface is charged to a given potential in a localized area.

26       When a given amount of a powdered drug is to be packaged, the charge and  
27       area of charge can be experimentally determined for each dose of drug and each  
28       particle size distribution. This can be done by controlling either the charged area for a  
29       given charge density or the total electrostatic charge on any individual charged area.

1 These conditions can be adjusted to provide the desired amount of the particular drug  
2 to be transferred at the transfer station.

3 Fig. 1 shows a schematic representation of the attraction of negatively charged  
4 powder particles to a support having a positive charge on the surface thereof.

5 Fig. 2 shows a block diagram of the various steps involved in practicing the  
6 invention.

7 Fig. 3 is a schematic representation of one form of drum type electrostatic  
8 device for transferring given small quantities of powdered drugs from an electrostatic  
9 attraction station, where a given quantity of powdered drug is attracted to and  
10 neutralizes a given charge on the drum, and a subsequent transfer station where the  
11 drug is transferred from the drum to a package therefor.

12 Figs. 4 and 5 are schematic functional representations of preferred components  
13 employed in the Fig. 3 type of apparatus.

14 Fig. 6 shows a different system wherein separate carriers, having micronized  
15 drug particles electrostatically attached to their surface, are used to carry the drug to  
16 the charged transfer surface.

17 Figs. 7 and 8 show methods of aerosolizing the powdered drug and ionizing  
18 the drug to give it a specific charge.

19 Fig. 9 shows a graph illustrating the percentage of suspended particles as a  
20 function of time and size, permitting creation of a suspended particle stream of any  
21 given desired size distribution.

22 Fig. 10 shows another embodiment of applying the aerosolized drug to a drum  
23 carrying charge "image".

24 Fig. 11 illustrates an ion projection system for creating the charge "image" on  
25 a dielectric surface.

26 Referring first to Fig. 1 there is illustrated a chamber 14 containing aerosolized  
27 dry powder particles 10. These particles 10 are suspended in air and carry a charge,  
28 for example a negative charge. Also in the chamber is a support surface 12 having a  
29 charge opposite to that on the particles. The support surface 12 will attract a number  
30 of charged particles 10 sufficient to neutralize the charge on the surface of the support

1       12. This support surface is one that can hold a discrete electrical charge on its surface,  
2       such as insulating material, e.g. plastic or a semiconductor material, such as selenium,  
3       used in the photocopy industry.

4           The actual amount of powder transferred to the carrier sheet is a function of  
5       the mass to charge ratio of the powdered particles. If one assumes surface charge  
6       saturation, the amount of charge carried by the particles is directly related to the  
7       surface area. For spheriodal particles, the charge varies as the square of the radius and  
8       the mass varies as the cube. Thus, the amount of charged particles picked up by a  
9       given portion of the surface of the charge carrier will be a function the total charge on  
10      the carrier. Thus, with a given surface charge density on the carrier, the amount of  
11      powder picked up is directly proportional to the charged area. Thus, for doubling the  
12      amount of powder to be picked up, the area on which charge is placed can be doubled.  
13      This can be used as a basic method to control the amount of powder to be picked by  
14      the carrier. Thus, for any particular powder or particle size distribution of powder, the  
15      exact area and amount of charge needed can be experimentally determined.

16           Referring now to Fig. 2, there is a schematic flow diagram of the various items  
17       of equipment needed to perform in the total process from powder supply to a sealed  
18       package containing a specified amount of powder in the package. At 16 is indicated  
19       the powder supply which is fed into a device 18 for creating an aerosol of the powder.  
20       Next the powder particles are ionized at 20. As will be indicated later, a number of  
21       these steps and pieces of equipment can be combined. At 24 is indicated a carrier  
22       surface capable of maintaining a space charge on its surface. This can be a plastic  
23       belt, for example, or a selenium drum of the type used in Xerox™ photocopiers. This  
24       carrier surface 24 is passed through a charging station 25 where predetermined  
25       electrostatic charge 25A (an electrostatic "image") is created on a predetermined area  
26       of the transfer surface. This charged surface 25A then passes through a step 26  
27       wherein powder 10 is deposited on the charged carrier surface in a sufficient amount  
28       26A to neutralize the charge carried by the carrier surface. Thereafter, the carrier  
29       surface, carrying the predetermined amount 26A of powder on its surface, is passed to  
30       a powder discharging device 30 which discharges the powder 26A from the surface 24

1 onto a packaging material 28, which may have indentations 29 for receiving the  
2 powder. The packaging material 28 containing its charge of powder 26A, then passes  
3 through a package sealing step 32.

4 As mentioned previously in discussing Fig. 1, the carrier surface with the  
5 electrostatic charge carries a known amount of charge on its surface and the polarity  
6 of this charge is opposite to that of the powder particles suspended in the chamber.  
7 The charged particles migrate to the charged surface because of the attraction by the  
8 opposite nature of the charges. This migration of the particles continues until the  
9 charge on the carrier surface is neutralized.

10 The actual amount of powder mass transferred to the carrier surface is a  
11 function of the mass to charge ratio of the charged particles. Although it is difficult to  
12 achieve a linear relationship between the mass and the actual charge, it is possible to  
13 establish a fixed relationship between the surface area of the powder particles and the  
14 charge the powder particle is carrying at charge saturation. However, the surface area  
15 of a mixed group of powder particles of different sizes and shapes can be extremely  
16 difficult to calculate mathematically, particularly when the shapes are irregular. (e.g.  
17 non spherical, microcrystalline, etc.) As mentioned earlier, the simplest method of  
18 determining the amount and area of charge to attract a given weight of particles is to  
19 estimate the correct area and charge and then apply the estimated charge to the  
20 estimated area on the carrier surface 24 and expose this selectively charged area to a  
21 mass of powder which has been ionized in the ionizing step. The amount of powder  
22 deposited can then be readily measured at the discharge step. Thereafter, either the  
23 size of the charged area or the amount of charge applied to the area at the charging  
24 station 25 can be adjusted upwardly or downwardly to provide the correct amount of  
25 charge, both in area and charge intensity, for picking up a desired weight of oppositely  
26 charged powder.

27 Referring now to Figs. 3, 4. and 5 one preferred apparatus for accomplishing  
28 the invention is illustrated schematically in Fig. 3, with details of the components  
29 thereof being shown in Figs. 4 and 5. The charge carrying surface is illustrated as a  
30 photo sensitive drum 24A which rotates between the charge "image" exposure 25

1 which creates a charge "image" 25A on the surface of the drum 24A. (see Fig. 4)  
2 This "image" exposure can be a light source e.g., a laser beam (or other controllable  
3 photon source), which is capable of creating an electrostatic "image" 25A on the  
4 surface of the drum of a desired size and charge density. The charge "image" 25A is  
5 then rotated to the image development station containing a bulk drug reservoir 78 and  
6 a high frequency vibrator 80 and an electrostatic defector 82 for producing an ionized  
7 cloud of drug powder which is attracted to the charge "image" 25 to neutralize charge  
8 in the "image", thus, forming a powder "image" 26A containing a predetermined  
9 amount of powder. (see Figs. 4 and 5) This powder "image" 26A is rotated to a drug  
10 transfer station 30 where it is released into the pockets 29 in the packaging layer 28.  
11 This transfer to the pockets 29 is accomplished, in one preferred embodiment, by the  
12 use of high voltage plate 56 (see Fig. 5) which overcomes the attraction of the charged  
13 "image" 25A on the surface of the drum, thus releasing the powder "image" 26A into  
14 the pocket 29. The pocket containing the predetermined quantity of drug is then  
15 passed through the sealing step 32.

16 Fig. 6 shows another embodiment of the invention wherein the micronized  
17 drug particles 10 are carried on the surface of discrete carriers 60 which can be small  
18 plastic beads, for example. When these plastic beads are contacted with an image  
19 25A, the micronized particles 10 are transferred to the charge "image" 25A on the  
20 surface of the drum 24A from the discrete carrier balls 60. To accomplish this, the  
21 positive charge on the image 25A should be higher than the positive charge on the  
22 surface of the individual carriers 60.

23 Figs. 7 and 8 show additional details of means for both handling drugs and  
24 providing aerosolization and ionization to provide a suspended stream of fine drug  
25 powders having a predetermined size and charge and for delivering same to a  
26 metering chamber 86. In Fig. 7 and 8, elements 16A, 18A and 20A and 16B, 18B and  
27 20B correspond to the equivalent elements in Figs. 2, 3 and 4.

28 Since repeatability is important for drug metering it is necessary to effectively  
29 address the issue of charge to mass variation with particle size.

1        One method of over-coming this problem is to control the particle size  
2        distribution in the drug powder. Fig. 8 shows one implementation to achieve this  
3        control of particle size. The voltage on the electrostatic deflector 82 is adjusted to  
4        control the particle sizes to be suspended in the holding chamber for delivery to the  
5        ionization chamber. Once the desired particle sizes are suspended they are drawn into  
6        the ionization chamber to ensure surface charge saturation on the particles. This will  
7        give a known charge to the mass ratio.

8        Fig. 7 shows an alternative means for controlling the size distribution. A high  
9        velocity air stream 84 is used to deaggregate and aerosolize the powder. The  
10        deaggregated powder is then contained in holding chamber 18A. The purpose of the  
11        holding chamber is to allow the larger size particles to settle, thereby producing a  
12        favorable particle size distribution. The particle size distribution is a function of the  
13        holding time as shown in Fig. 9. The suspended particles are then ionized and  
14        exposed to the charge image as shown in at 26 in Fig. 3

15       Fig. 9 shows the percentage of particles sizes suspended in a holding chamber  
16       as a function of time. Such a chamber may be provided with a slow upward flowing  
17       air current to maintain the aerosol suspension. As can be seen, the percentage of  
18       suspended particles is very largely determined by particle size (where S equals small  
19       particle sizes, M equals medium particle sizes and L equals large particle sizes).  
20       Through experiment one can select a time slot T that will give the desired particle size  
21       distribution for any particle drug dosage. Additionally, or in place of settling time,  
22       one or more filters can be used for obtaining a given particle size range.

23       Fig. 10 is similar to Figure 4 except that the Image Development Station 26 in  
24       this figure is replaced with the Stationary electrode 26B and an air passageway 50 for  
25       carrying the aerosolized powder. The rotating drum 24 has a dielectric or  
26       photoreceptor surface on to which is deposited the latent image. As an example the  
27       aerosolization chamber would be similar to that shown in Figure 7. The metering  
28       chamber in Figure 7 is then the air-passageway 25 between the dielectric surface 24  
29       and the stationary electrode 26B, with a bias voltage V applied between surface 24  
30       and electrode 26B. The undeposited powder then exits at the right side of this air-

1 passageway to be collected for later use or recirculated back into the aerosolization  
2 chamber.

3 Figure 11 above shows an ion projection print head where an ion beam is used  
4 to produce a charge "image" on a dielectric surface. The corona wire 52 has a high  
5 voltage applied to it which causes the air to breakdown and produces the ions 52A  
6 necessary for the operation of the ion projection printers. The remainder of the ion  
7 projection print head includes the usual control electrode 54, screen electrode 56 and  
8 insulator 58. The relative potential that is applied to the control and screen electrodes  
9 then regulates the amount of ions 25C that will be metered and deposited on to the  
10 dielectric surface 24 these ions being deposited on the surface to form the latent image  
11 25A. Both the intensity and size of the ion beam can be adjusted as will be apparent  
12 to one of ordinary skill in the art. The advantage of this system is that it does not  
13 require a photosensitive surface and can therefore be rugged making it suitable for the  
14 manufacturing environment.

15 The invention also may be advantageously employed for forming pills of  
16 microgram quantities of a drug by printing on a substrate an "image" formed of  
17 discrete dots of finely divided drug particles. the quantity of particles in a dot  
18 corresponding to a given quantity of drug, and packaging one or more of the dots as a  
19 predetermined therapeutic drug dose.

1

CLAIMS

2        1. The method of packaging powder characterized by the steps of developing  
3        a predetermined electrostatic charge having a predetermined "image" area on a  
4        powder carrier surface, contacting said carrier surface with a sufficient amount of  
5        powder to neutralize said charge, moving said powder and said surface to a transfer  
6        station, transferring said powder to said package and sealing a package to contain a  
7        amount of transferred powder.

8        2. The method of claim 1, characterized in that said predetermined charge  
9        and area on said carrier surface are estimated, said estimated electrostatically charged  
10       area is then exposed to said powder of opposite charge and the amount of powder  
11       attracted to said predetermined area is measured, thereafter necessary adjustments to  
12       the amount of charge and/or the area is made to attract the predetermined desired  
13       amount of powder to said "image" area.

14       3. The method of claim 1, characterized in that the charge "image" is  
15       produced by an ion beam whose intensity and/or area can be varied, or by a photon  
16       beam whose intensity and/or area can be varied.

17       4. The method of claim 3, characterized by the step of controlling particle size  
18       distribution of particles in the powder deposited on the charge "image".

19       5. The method of claim 1, characterized in that pills of predetermined  
20       therapeutic drug dose are formed by printing on a substrate an "image" formed of  
21       discrete dots of finely divided drug particles, the quantity of particles in a dot  
22       corresponding to a given quantity of drug, and packaging one or more of said dots as a  
23       predetermined therapeutic drug dose.

24       6. Apparatus for packaging for powder characterized by comprising:  
25       a source of powder 16;

26       a powder carrier surface 24;

27       means 26 for applying a predetermined electrostatic charge to a predetermined  
28       area of said carrier surface, to create a charge "image" 25A on said surface;

29       means 26 for applying to said powder an electrostatic charge opposite to that  
30       of said electrostatic charge on said carrier surface;

1       means for exposing said charged area of said area on said carrier surface to  
2       charged powder to create a powder "image" 26A on said carrier surface;

3       means 30 for transferring said powder adhering to said carrier surface to a  
4       transfer system and neutralizing said electrostatic charge on said carrier surface to  
5       cause the powder to transfer into a package 28 therefor; and,

6       means 32 for sealing said package.

7       7. The apparatus of claim 6, characterized in that the means for placing the  
8       electrostatic "image" on the carrier surface is adjustable both in intensity and area so  
9       that the exact amount of electrostatic charge and area thereof can be controlled.

10       8. The apparatus of claim 6, characterized by additionally including a means  
11       to control the powder particle size distribution to ensure repeatability and accuracy of  
12       powder metering.

13       9. The apparatus of claim 8, characterized by further comprising a high  
14       frequency vibrator 80 for deaggregating the powder, and an electrostatic potential  
15       means 82 for aerosolizing the particle size distribution of interest.

16       10. The apparatus of claim 6, characterized by a high velocity air stream 84  
17       for deaggregating and aerosolizing the powder particles, and a holding chamber 18B  
18       for controlling the particle size distribution in the air stream using particle settling  
19       times.

20       11. The apparatus of claim 6, characterized in that the charge "image" is  
21       produced by an ion beam whose intensity and/or area can be varied, or by a photon  
22       beam whose intensity and/or area can be varied.



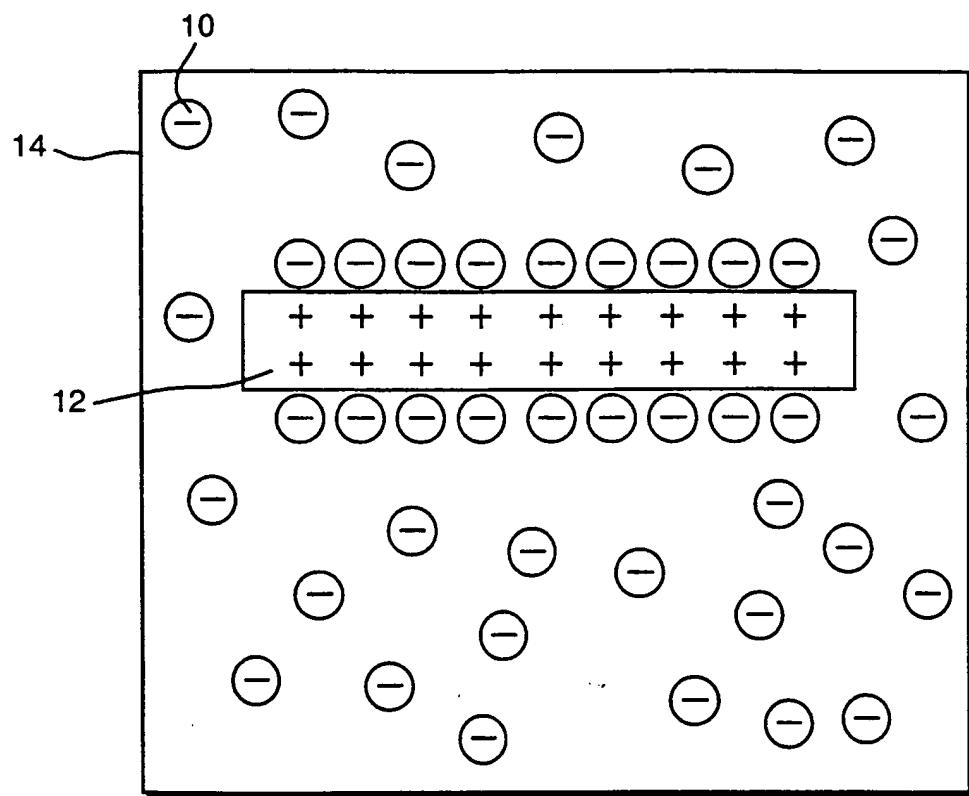
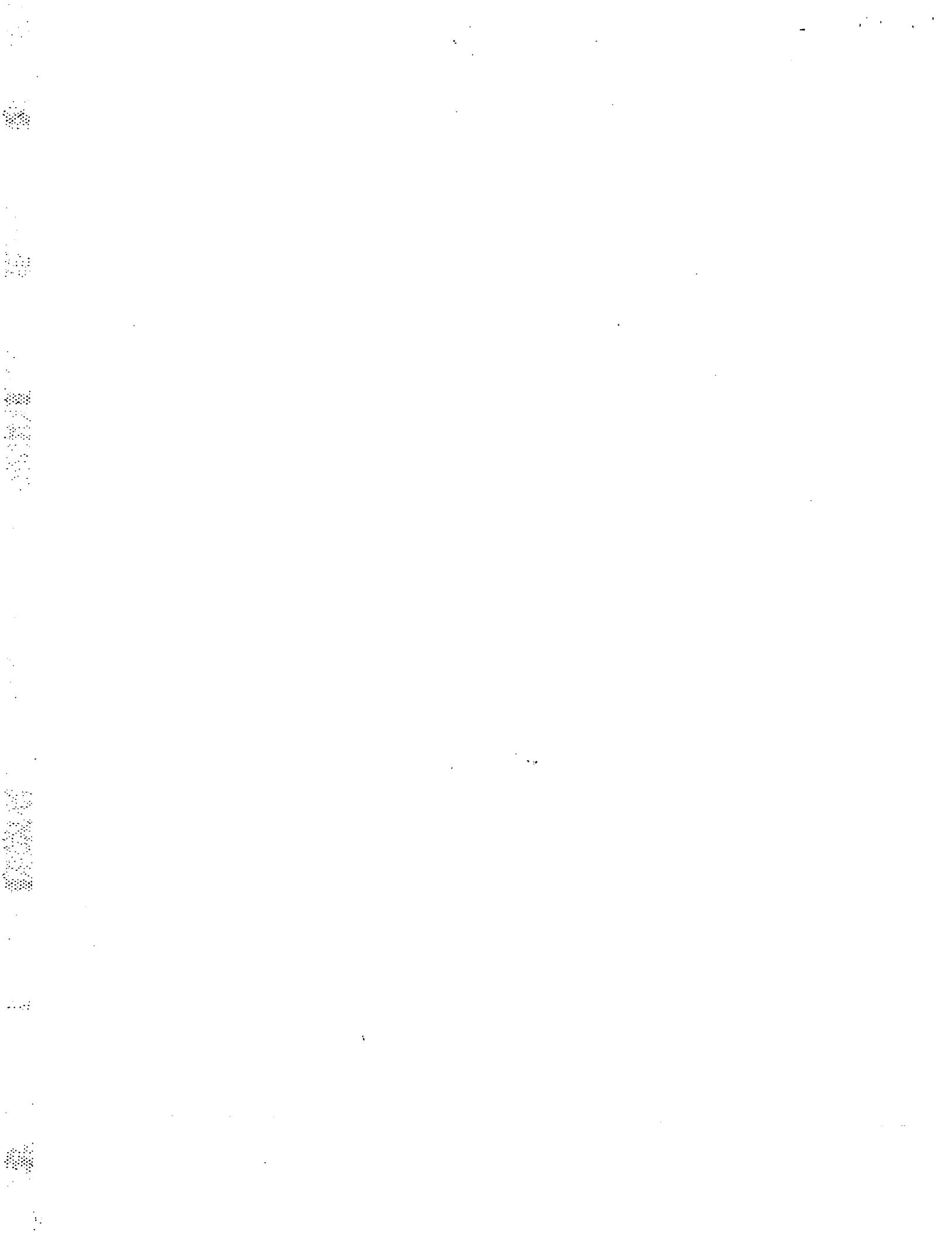


FIG. 1



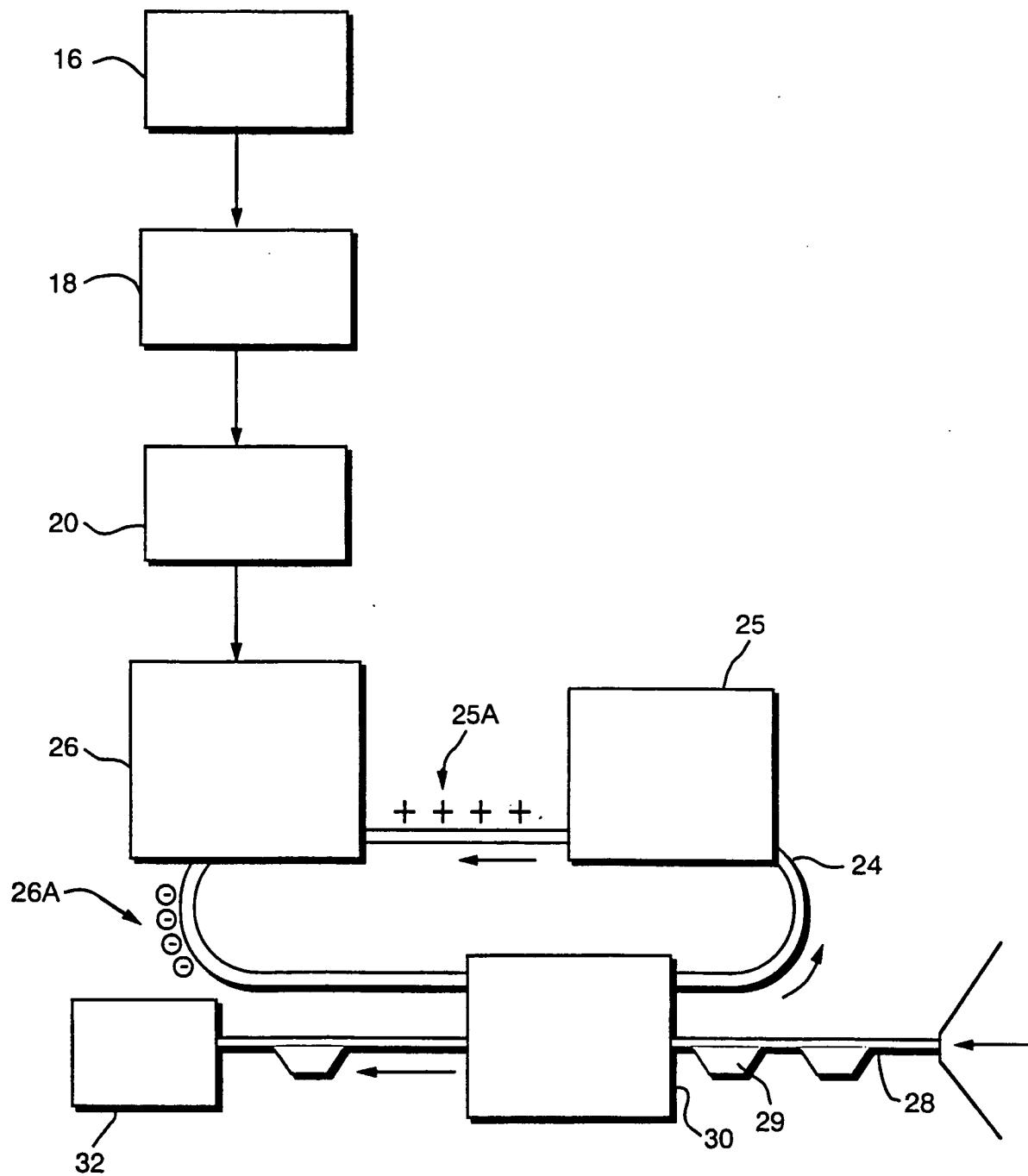
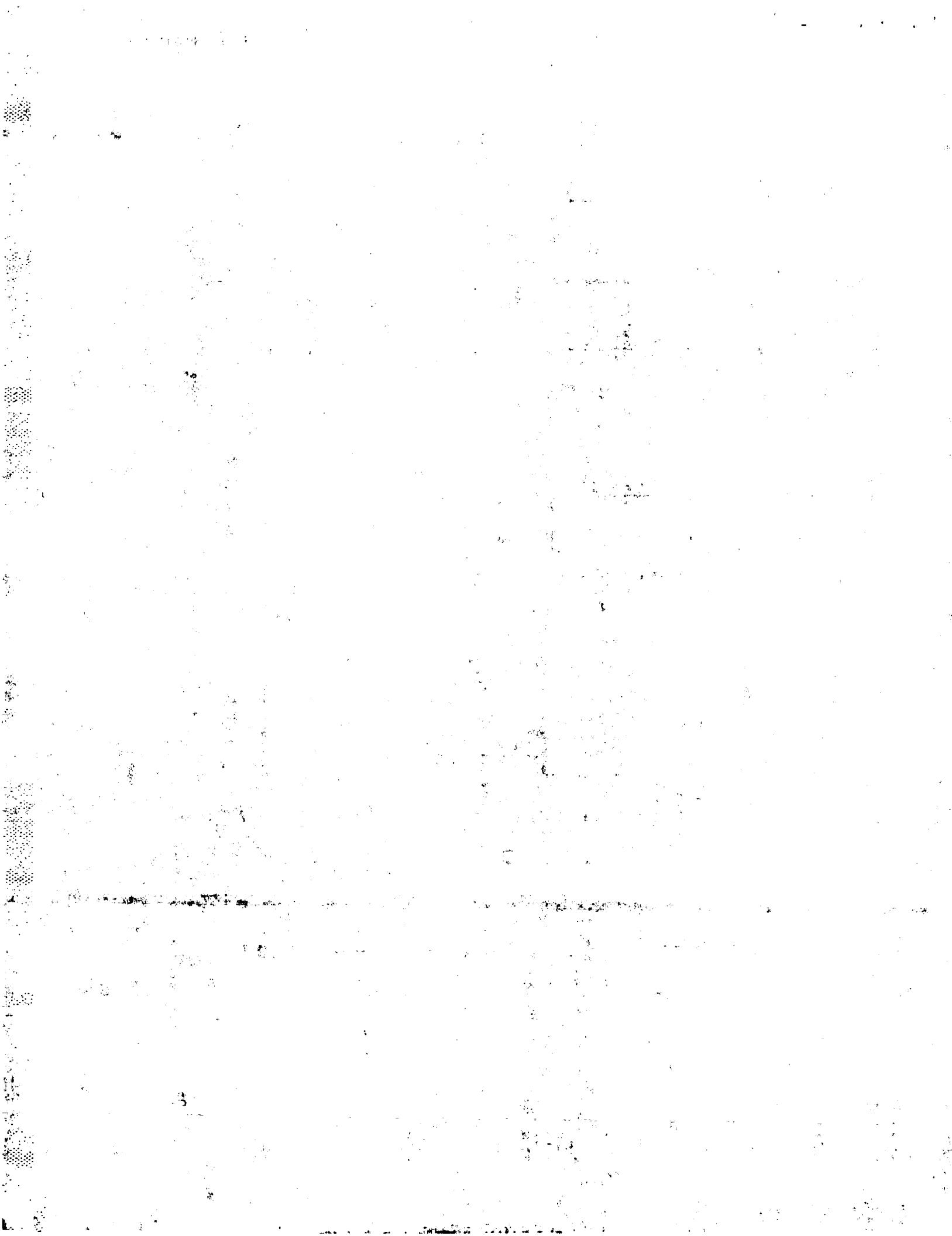


FIG. 2



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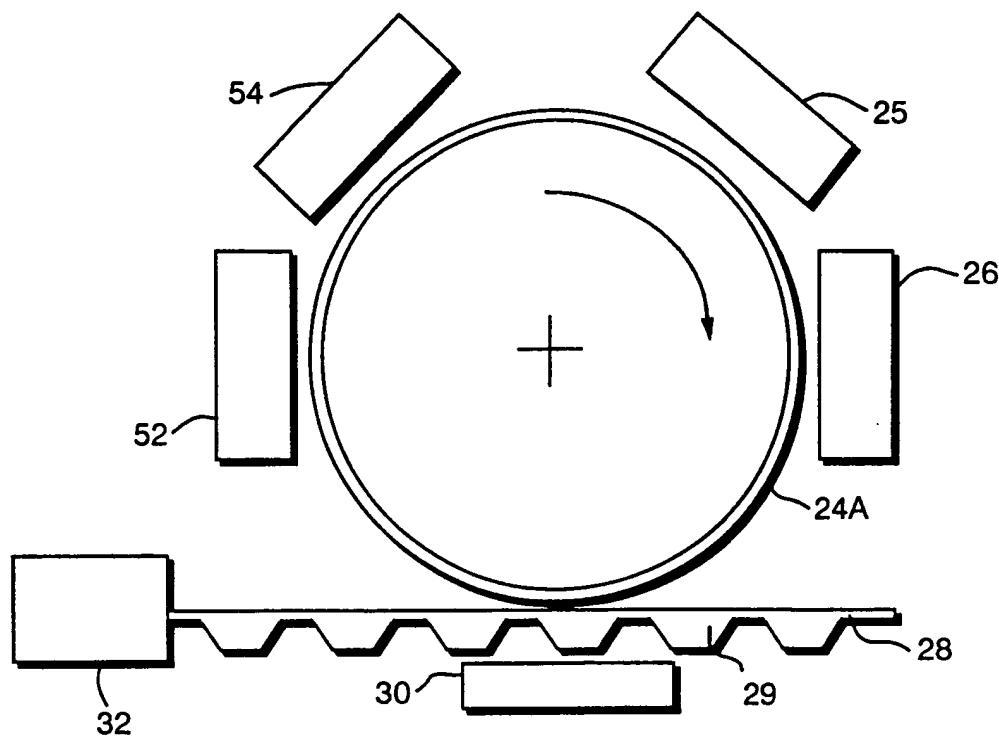


FIG. 3

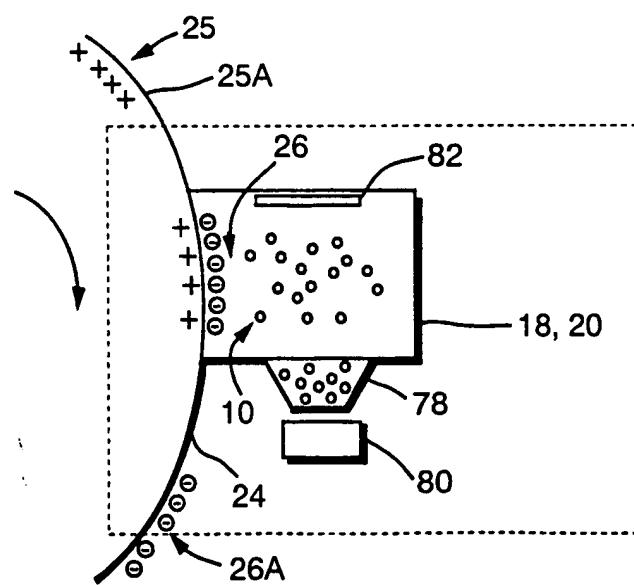
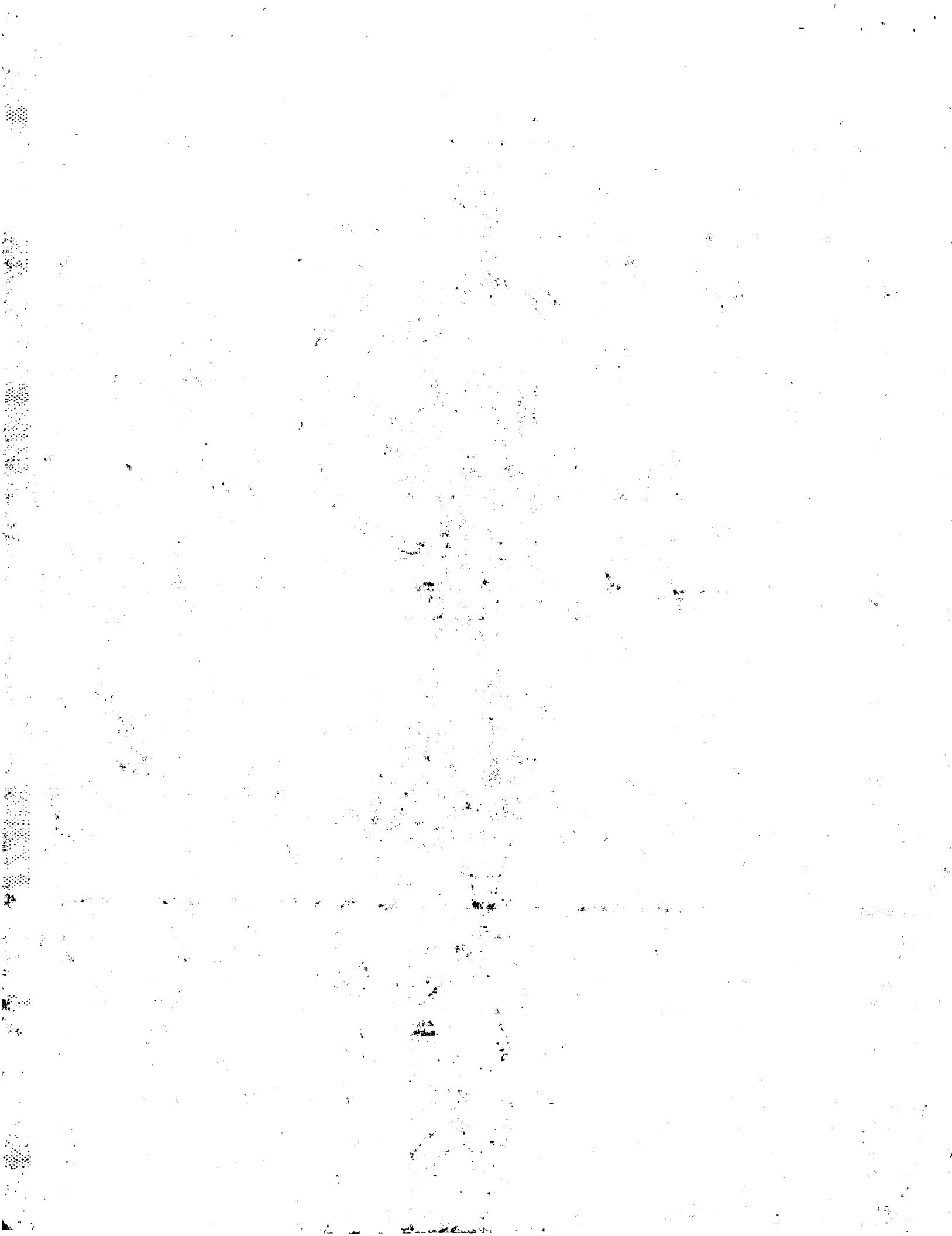


FIG. 4



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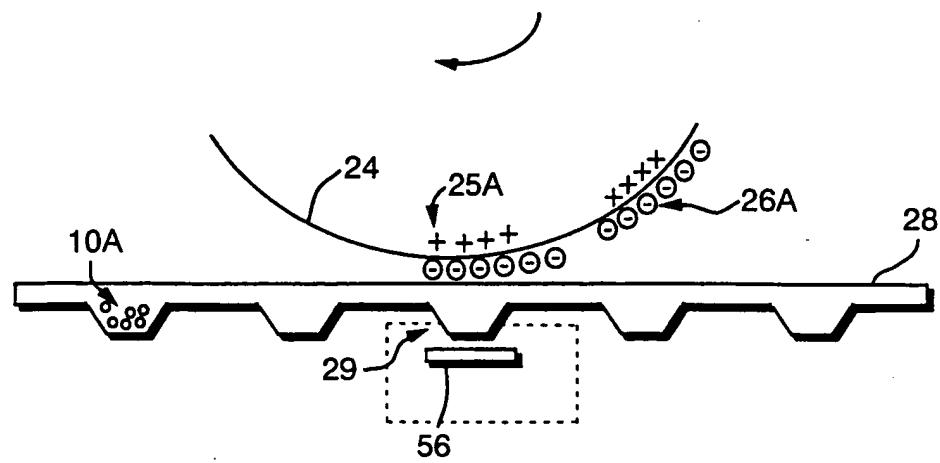


FIG. 5

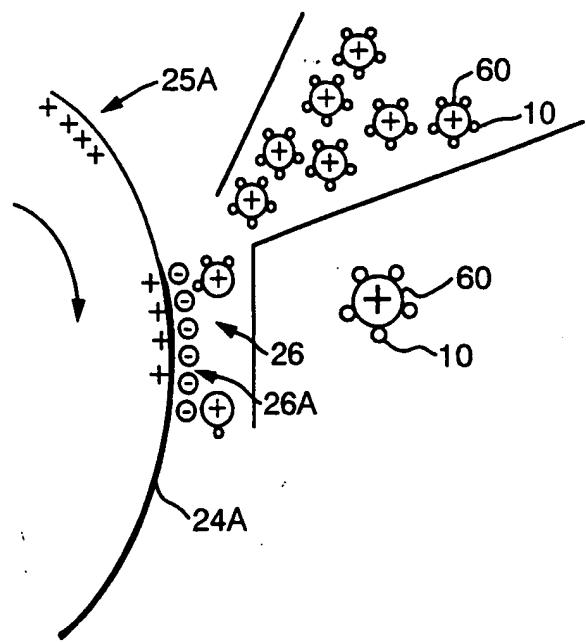
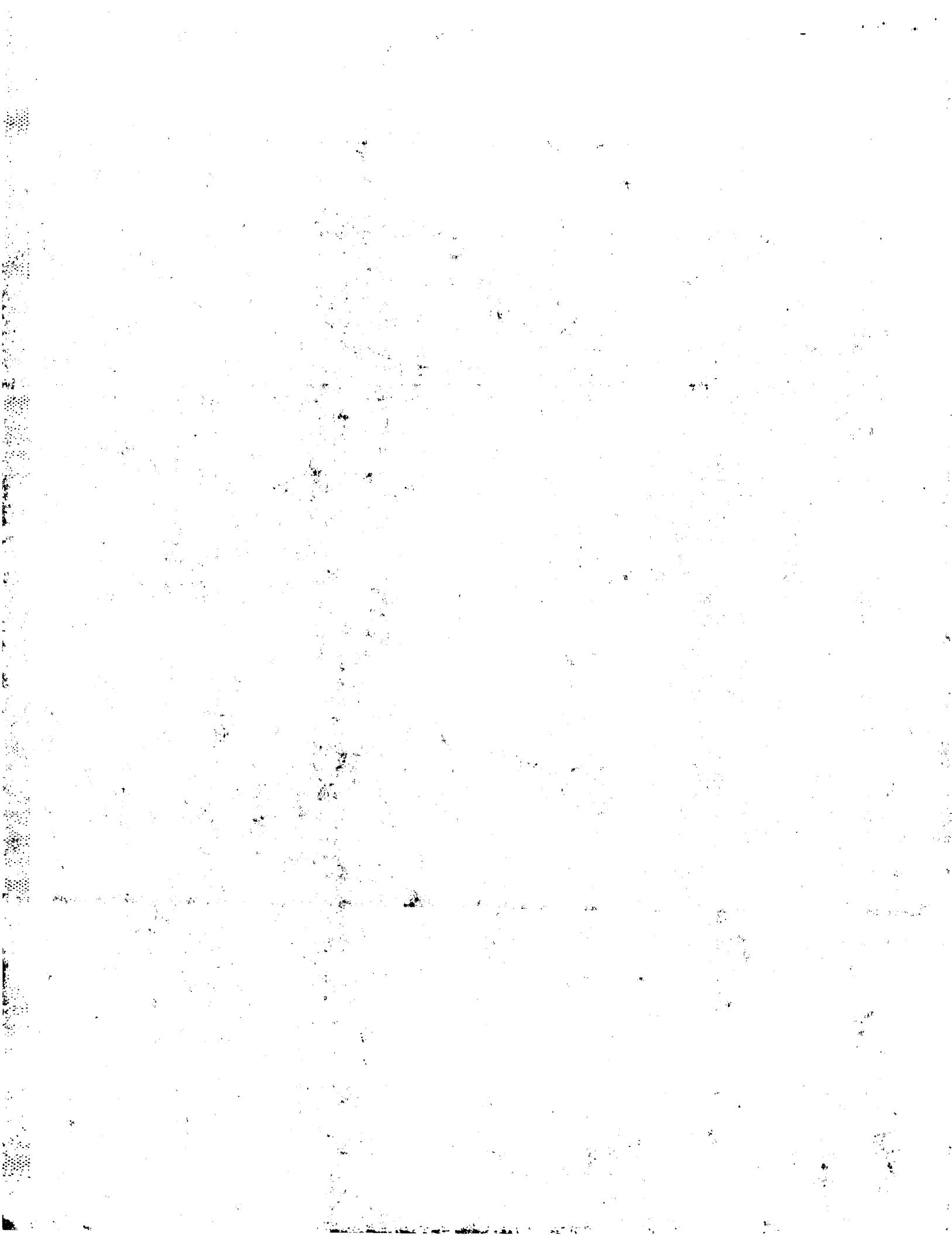


FIG. 6



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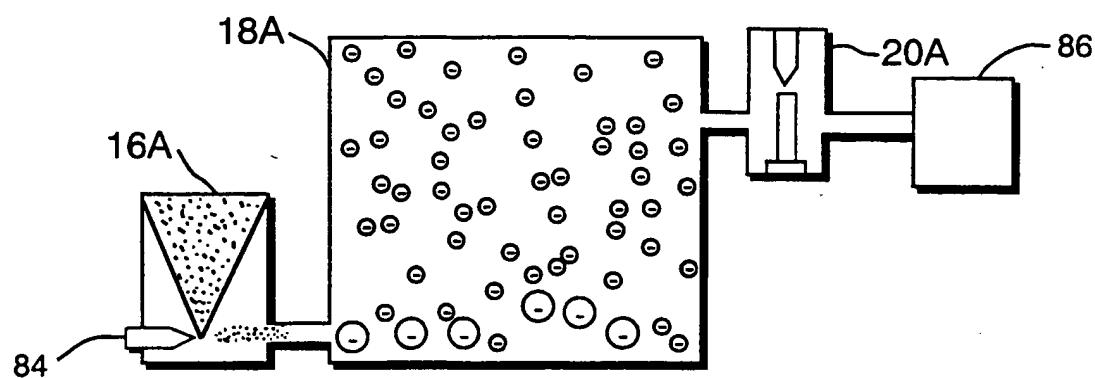


FIG. 7

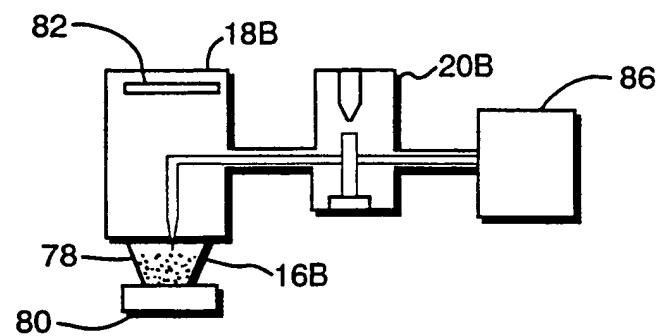


FIG. 8

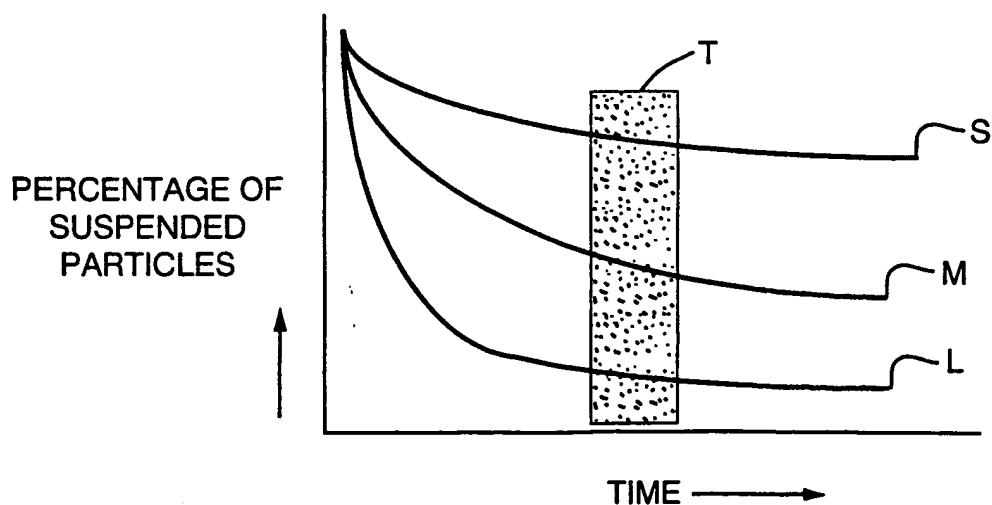
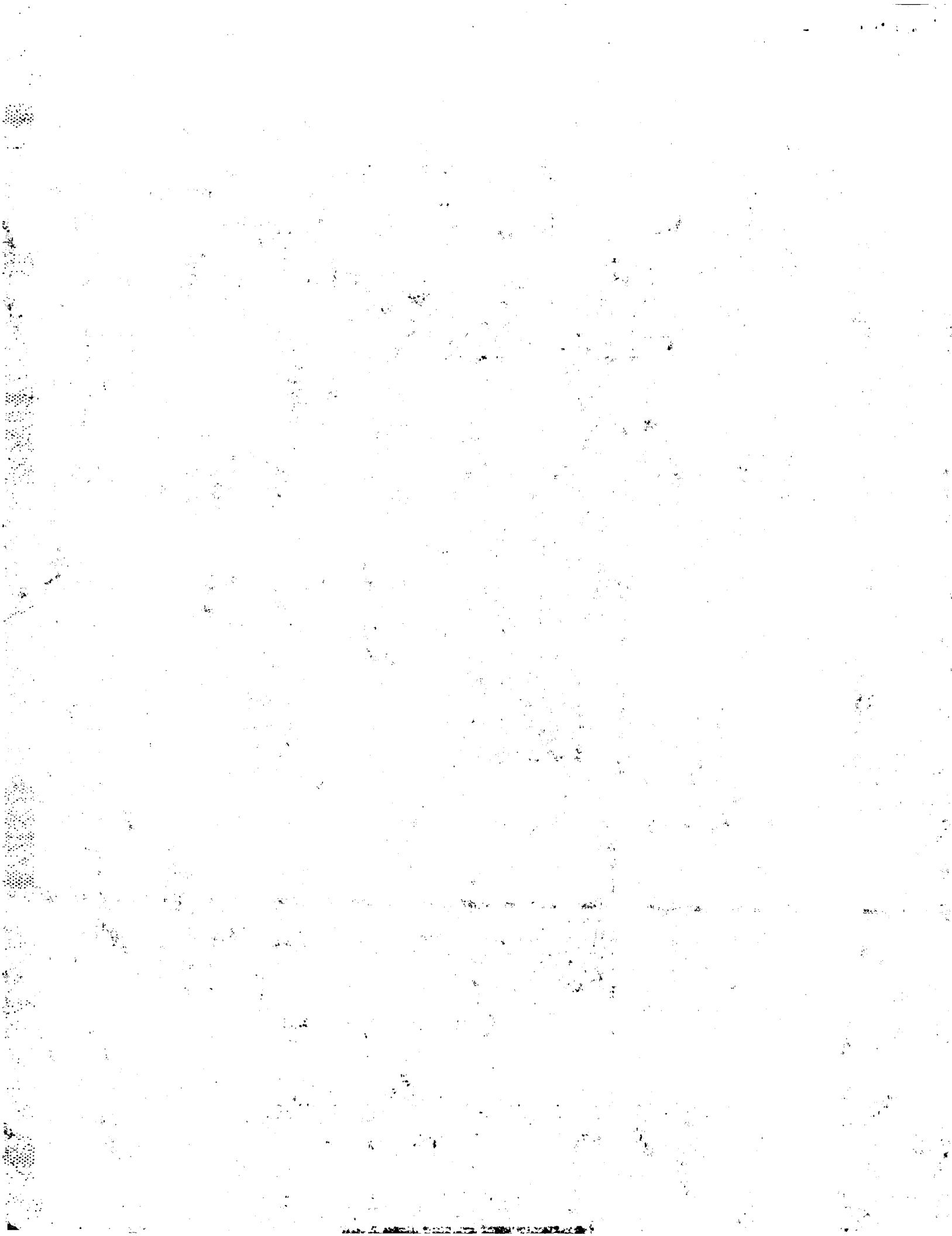


FIG. 9



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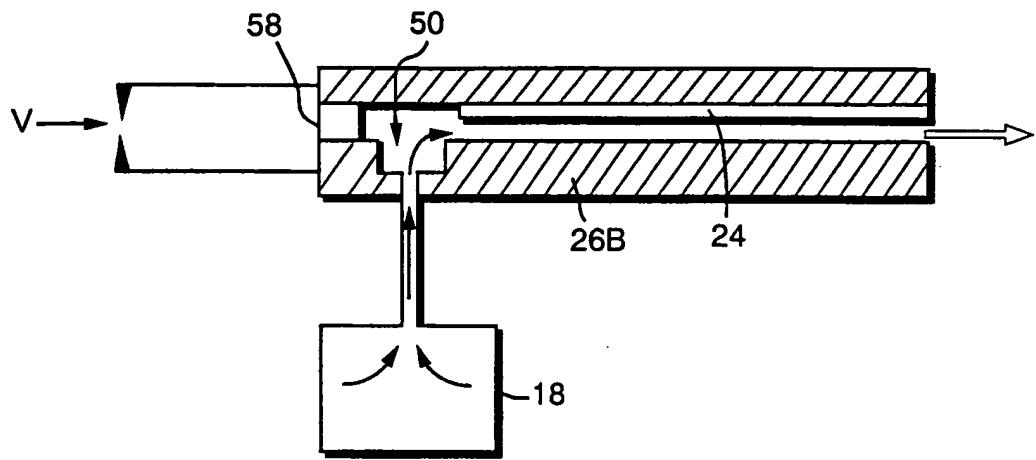


FIG. 10

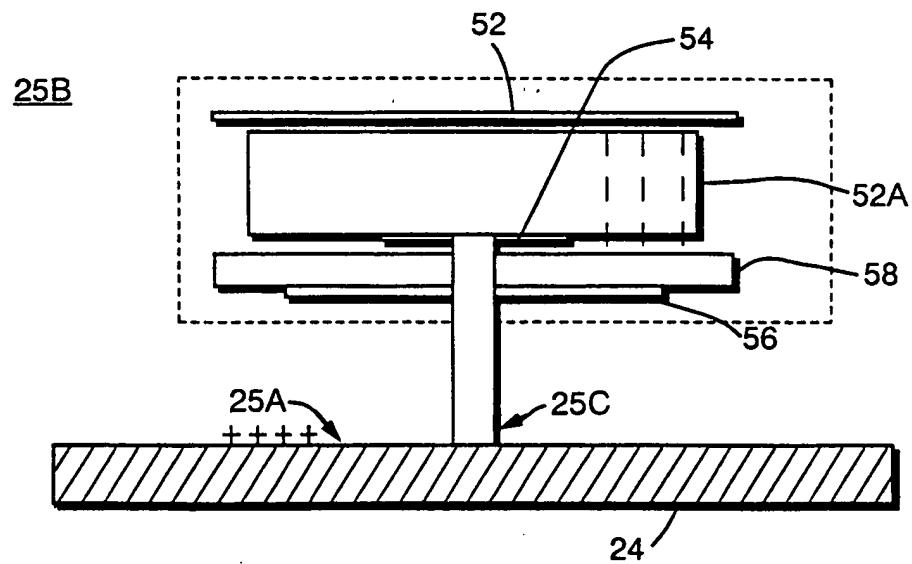


FIG. 11



## INTERNATIONAL SEARCH REPORT

International application No.

PCT/US97/10494

## A. CLASSIFICATION OF SUBJECT MATTER

IPC(6) :B65B 1/30

US CL :Please See Extra Sheet.

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 53/428, 111.R, 235, 467, 473, 266.1, 502, 503; 141/DIG.1; 198/690.1, 691

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 3,241,625 A (SOOJIAN) 22 March 1966, entire document.	
A	US 3,437,074 A (HAGOPIAN et al) 08 April 1969, entire document.	
A	US 4,021,587 A (BANKER) 03 May 1977, entire document.	
A	US 4,170,287 A (EDWARDS et al) 09 October 1979, entire document.	
A	US 4,252,434 A (NAKAMURA et al) 24 February 1981, entire document.	
A	US 4,555,174 A (KRAMER) 26 November 1985, entire document.	

Further documents are listed in the continuation of Box C.  See patent family annex.

*A*	Special categories of cited documents:	*T*	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
*E*	document defining the general state of the art which is not considered to be of particular relevance	*X*	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
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Date of the actual completion of the international search

24 JULY 1997

Date of mailing of the international search report

07 AUG 1997

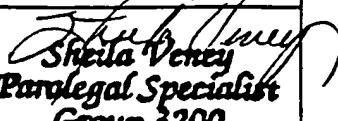
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**INTERNATIONAL SEARCH REPORT**

International application No.

PCT/US97/10494

**C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT**

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 4,848,267 A (SLAYTON et al) 18 July 1989, entire document.	

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US97/10494

A. CLASSIFICATION OF SUBJECT MATTER:  
US CL :

53/428, 111.R, 235, 467, 473, 266.1, 502, 503; 141/DIG.1; 198/690.1, 691

